OIPE
MAY 10 2002
PATENT & TRADEMARK OFFICE

CLAIMS

What is claimed is:

1. A process for the screen, identification or prediction, and assembly of 19-25nt double-stranded oligonucleotides as active pharmaceutical compositions for the treatment of a variety of viral infection, malignant tumors, and genetic and metabolic diseases, which includes the following steps:

   A) screening the disease-causing genes, over-expressing in cells and/or tissues, with the gene-chip and protein-chip microarrays,

   B) identifying a specific DNA sequence within the abnormal gene encoding a protein or playing other biological roles with the assistance of computer and specific software,

   C) predicting efficacious 19-25nt double-stranded oligonucleotides with a 5'-AU(T)CCG -3' or 5'-U(T)CCCG -3' special pattern complementary to at least a portion of a RNA molecule, and

   D) making sure that selected sequence is not localized within the stem-loop of target mRNA with any related software.

2. The process according to claim 1, wherein identifying specific DNA sequences in the human genome includs the steps of:

   (a) identifying endogenous short interfering RNA (siRNA) sequences in the human genome with the assistance of computer and specific software,

   (b) searching candidate sequence with conserved patterns from the same gene family in different species by using multiple sequence alignment and pattern discovery algorithm as well as Blast searches of Genebank,

(c) selecting a specific DNA sequence with the length of 19-25 nucleotides which is 100% homologous to most, if not all, members of this gene family in human genomic databases,

(d) valuating the specific 19-25nt sequence by the standard in which there is minimal similarity to any other gene families and 95-100% homologous to any members of the same human gene family through Blast Alignment of Genebank.

3. The process according to one of claims 2, wherein the special pattern such as 5'-CGGAU-3' is a critical portion of a specific 19-25nt sequence, which is the base for selecting a region in a given genomic RNA as both a target and a drug.

4. The process according to claim 1, 2 or 3, wherein the 19-25nt double-stranded oligonucleotides may be a 19-25nt dsRNA, a 19-25nt sRNA-cDNA, or a 19-25nt dsDNA.

5. The process according to claim 4, wherein the cDNA in said sRNA-cDNA is an antisense oligonucleotide, while sRNA is related to a sense oligonucleotide.

6. The process according to claim 1, 2, 3 and 4, wherein the 19-25nt double-stranded oligonucleotides can specifically hybridize with at least a 19-nucleobase portion of an active site on a nucleic acid molecule encoding a protein or playing other functions, and interfere with or shut off target RNAs, and/or regulate the DNA methylation of corresponding regions of genome derived from human and other species.

7. The process according to claim 2, wherein said endogenous RNAi is a sequence occurring in an intergenetic area or an intron region, where a 19-25nt stem-loop structures can be identified.

8. The process according to claim 6, wherein target RNAs include mRNA or other types of RNA molecules.

9. Pharmaceutical compositions of gene drugs such as Dermogene, Lungene, Hepatogene, Leukogene, Lymphogene, Prostogene, Breastogene Braintumogene and Skin-whitogene including but being not limited to part or all of the following components:

- single or a group of specific 19-25nt dsRNA, 19-25nt sRNA-cDNA, 19-25nt dsDNA and / or single-stranded RNA and / or DNA with the special pattern, 5'-CGGAT(U)-3' or its derivative sequences,
- one or more nucleic acid condensation agents, or none,
- one or more pharmaceutically acceptable carriers,
- one or more specific cell-targeting proteins, and
- other active agents and additional materials.

10. A pharmaceutical composition according to claim 9, wherein the 19-25nt double-stranded oligonucleotides with the special pattern such as 5'-CGGAU-3' or other 5'-CGGNN-3' can efficiently inhibit expression of a gene in an animal, especially a human.

11. A pharmaceutical composition according to claim 9 wherein a group of oligonucleotides are more than one double-stranded oligonucleotides, each of which is complementary to the specific target sequence within a given RNA.

12. The compositions of gene drugs according to claim 1 and 9, wherein the double-stranded oligonucleotides have a cleavage pattern comprising SEQ ID #: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51.

13. The compound of gene drugs according to claim 1 and 9, wherein the mixture comprises at least one double-stranded oligonucleotide molecule, or different double-stranded oligonucleotides, different dose of the same agent, or any combination thereof.

14. The compound of claim 1, 9 and 13, wherein the double-stranded oligonucleotides can contain at least one special pattern which can be localized in any place in an oligonucleotide sequence.

15. The compound of claim 1, 9, 13 and 14, wherein the special pattern in the antisense strand of SDSO or antisense oligonucleotide (ASO) molecule includes but be not limited to AU(T)CCG, U(T)U(T)CCG, GU(T)CCG, CU(T)CCG, GCCCG, U(T)CCCG, ACCCG, CCCCG, AACCG,

U(T)ACCG, GACCG, CACCG, AGCCG, GGCCG, CGCCG, and U(T)GCCG in the order of 5' to 3'.

16. The compound of claim 1, 9, 13 and 14, wherein the double-stranded oligonucleotides can be a chimeric oligonucleotides.

17. A composition comprising the compound of claim 9 and a pharmaceutically acceptable carrier or diluents.

18. The composition of claim 9 and 17 further comprising a colloidal dispersion system.

19. A simplified method for predicting and selecting a specific and efficacious SDSO or antisense oligonucleotide (ASO) molecules, which includes the identification of a special pattern which can be localized in any position of an oligonucleotide sequence and the evaluation of the specificity of a selected sequence.

20. A composition comprising of the compound of gene drugs such as Dermogene, Lungene, Hepatogene, Leukogene, Lymphogene, Prostogene, Breastogene and Braintumogene as well as cosmetics such as Skin-whitogene.